

## **Acambis reports positive data from trials of universal influenza A vaccine**

**Cambridge, UK and Cambridge, Massachusetts – 3 January 2008** – Acambis plc (Acambis) (LSE: ACM), a leading vaccine development company, announces preliminary results from a Phase 1 clinical trial and a pre-clinical challenge study of its ACAM-FLU-A™ vaccine.

ACAM-FLU-A™ is a recombinant vaccine linked to a Hepatitis B core protein. It targets M2e, a conserved region of all influenza 'A' strains. This approach could overcome the need for annual vaccine reformulations and, since all pandemic influenza strains are type 'A', it could also be a potential vaccine against pandemics.

The Phase 1 trial of ACAM-FLU-A™ evaluated the vaccine's safety and ability to generate an immune response. The randomised, double-blind, placebo-controlled trial was conducted at multiple centres in the US and involved 79 subjects. The study consisted of four arms – ACAM-FLU-A™ alone, ACAM-FLU-A™ plus aluminium hydroxide adjuvant, ACAM-FLU-A™ plus QS-21 adjuvant and placebo – and the subjects received two doses. QS-21 Stimulon® adjuvant is an investigational adjuvant (immune stimulant) provided under an option agreement with Antigenics Inc., which has recently been converted to a non-exclusive licence and supply agreement.

The trial results demonstrate that ACAM-FLU-A™ is well tolerated and immunogenic. Whilst immune responses were seen in all vaccinated groups, the highest immune responses occurred in the group vaccinated with ACAM-FLU-A™ plus QS-21. In this group, 90% of subjects seroconverted.

In parallel with the Phase 1 trial, Acambis has conducted a pre-clinical study to test whether an M2e-based vaccine could protect against the Vietnam 2004 strain<sup>(1)</sup> of H5N1 avian influenza (bird flu). The H5N1 virus was lethal in the placebo-treated group, whereas 70% of those in the group vaccinated with the M2e-based vaccine from the same influenza strain were protected.

Acambis plans to submit these results for publication in due course.

Ian Garland, Chief Executive Officer of Acambis, said:

"We are very excited about these new data and believe that this highly innovative vaccine could be very attractive in such a competitive field. We will explore partnering in parallel with continued development of ACAM-FLU-A™."

Michael Watson, Acambis' Executive Vice President, Research & Development, added:

"M2e is one of the most discussed new approaches for influenza vaccination. These are exciting data as they show that our ACAM-FLU-A™ vaccine can generate a robust M2e antibody response and that M2e-based vaccines can protect against H5N1 avian influenza. We believe that these results confirm we have an approach worthy of further development."

Influenza is a major global threat, which the WHO estimates causes between 250,000 and 500,000 deaths every year around the world<sup>(2)</sup>. Currently, influenza vaccines are reformulated each year to address virus mutations.

Acambis' vaccine candidate, which is protected by extensive intellectual property, was developed using technology licensed from VIB that was invented by Walter Fiers, Emeritus Professor of the VIB Department for Molecular Biomedical Research at the University of Ghent, Belgium.

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## Editor's notes

### About the influenza virus and influenza vaccines

Today, seasonal influenza represents the single largest vaccine market in the world, worth an estimated \$2.2bn and projected to grow to \$4bn by 2010<sup>(3)</sup>. It is still a major global threat, which the WHO estimates causes between 250,000 and 500,000 deaths every year around the world<sup>(2)</sup>. Immunity against influenza viruses, whether acquired by natural infection or immunisation, is typically transient due to the virus's ability to mutate and evade pre-existing immunity. Accordingly, current licensed vaccines are updated on an annual basis to target most effectively the presently circulating strains.

Pandemic influenza viruses are sufficiently distinct from seasonal epidemic viruses that new vaccines must be developed to address them. Pandemic influenza vaccines, primarily targeting avian H5N1 viruses, are being stockpiled for emergency use. However, the efficacy of these vaccines may be negatively impacted by continual mutations in circulating H5N1 strains. Experts believe the next pandemic could cause disease in two billion people. Based on best-case scenarios modelled on the mild pandemic of 1968, this could result in two to seven million deaths. However, if the death toll associated with the 1918 influenza virus were applied to today's world population, there could be 180 million to 360 million deaths globally<sup>(4)</sup>.

### About ACAM-FLU-A™

ACAM-FLU-A™ is a recombinant vaccine that uses a hepatitis B core protein (HBc) to present M2e, the extracellular domain of the ion channel protein M2<sup>(5)</sup>. M2 is one of the three proteins expressed on the surface of the 'A' strain influenza virus and of infected cells alongside haemagglutinin (HA) and neuraminidase (NA). Unlike HA and NA, M2 is highly conserved, albeit under natural conditions not easily recognised by the immune system. M2e could elicit an immune response to all influenza 'A' strains. As such, ACAM-FLU-A™ has the potential to be both a universal pandemic or pre-pandemic influenza vaccine and part of a universal seasonal vaccine. Historically, influenza pandemics have been caused by 'A' strains of the virus while seasonal vaccines target both 'A' and 'B' strains of the virus.

## References

(1) *The Vietnam 2004 Clade 1 avian influenza virus has been used by manufacturers to develop and produce pre-pandemic vaccines.*

[http://www.who.int/csr/disease/avian\\_influenza/guidelines/recommendationvaccine.pdf](http://www.who.int/csr/disease/avian_influenza/guidelines/recommendationvaccine.pdf)

(2) WHO: <http://www.who.int/mediacentre/factsheets/fs211/en/>

(3) *Datamonitor*

(4) *Kamps-Hoffmann-Preiser, Influenza Report 2006*

(5) *Neirynck et al., Nature Medicine, 5, 1157, 1999*

### About Acambis

Acambis is a leading vaccine company developing novel vaccines that address significant unmet medical needs or substantially improve standards of care. ChimeriVax™-JE, Acambis' most advanced product in its development-stage pipeline, has to date shown an excellent safety and efficacy profile following pivotal Phase 3 trials. It is currently undergoing paediatric trials in India and is partnered with Sanofi Pasteur and Bharat Biotech. Acambis' proprietary ChimeriVax™ technology, developed in association with St Louis University, has also been used to develop ChimeriVax™-West Nile, which is undergoing Phase 2 clinical testing, making it the most advanced investigational vaccine against the West Nile virus. Acambis has established a global collaboration with Sanofi Pasteur for further development and commercialisation of the

vaccine. ChimeriVax™ has also been applied to development of Sanofi Pasteur's tetravalent dengue vaccine, which has successfully demonstrated proof-of-concept in a Phase 2 trial by generating 100% seroconversion to all four dengue virus serotypes.

Acambis also has the only vaccine in development against *Clostridium difficile* bacteria, a leading cause of hospital-acquired infections. *C. difficile* is estimated to cause at least 360,000 cases of *C. difficile*-associated disease in the US alone with annual costs to the healthcare system of \$3.2bn. Acambis' influenza programme aims to develop a universal vaccine against influenza, for which a universal 'A' strain vaccine, ACAM-FLU-A™, has completed a Phase 1 trial. It also includes various further vaccine candidates in the research and pre-clinical stages.

Acambis is recognised internationally as the leading producer of smallpox vaccines. Acambis' ACAM2000™ (Smallpox (Vaccinia) Vaccine, Live) vaccine for active immunisation against smallpox disease for persons determined to be at high risk for smallpox infection was licensed by the US Food and Drug Administration in August 2007. Acambis has manufactured doses of ACAM2000™ for emergency-use stockpiles held by the US Government and several other governments around the world. For safety and prescribing information, please refer to [www.acambis.com/ACAM2000](http://www.acambis.com/ACAM2000).

Acambis is based in Cambridge, UK and Cambridge, Massachusetts, US, and is listed on the London Stock Exchange (ACM). More information is available at [www.acambis.com](http://www.acambis.com).

**“Safe Harbour” statement**

Statements contained within this news release may contain forward-looking comments, which involve risks and uncertainties that may cause actual results to vary from those contained in the forward-looking statements. In some cases, you can identify such forward-looking statements by terminology such as 'may', 'will', 'could', 'forecasts', 'expects', 'plans', 'anticipates', 'believes', 'estimates', 'predicts', 'potential', or 'continue'. Predictions and forward-looking references in this news release are subject to the satisfactory progress of research which is, by its very nature, unpredictable. Forward projections reflect management's best estimates based on information available at the time of issue.